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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re the application of: Curtis, Rory A.J.

Serial No.: 09/587,111

Filed: June 2, 2000

For: NOVEL MEMBERS OF THE  
CAPSAICIN/VANILLOID RECEPTOR FAMILY OF  
PROTEINS AND USES THEREOF

Attorney Docket No.: MNI-062CP2DV1

Group Art Unit: 1646

Examiner: Ulm, J. D.

Commissioner for Patents

Box AF

Washington, D.C. 20231

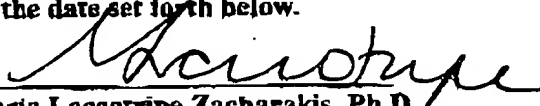
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I hereby certify that this correspondence is being facsimile transmitted to the Commissioner for Patents,  
Box AF, Washington, D.C. 20231 on the date set forth below.

By:

4/11/03

Date of Signature

  
Maria Laccorripe Zacharakis, Ph.D.  
Attorney for Applicant  
Limited Recognition Under 37 C.F.R. 10.9(b)

**DECLARATION PURSUANT TO 37 CFR §1.131**

Dear Sir:

I, Rory A.J. Curtis, a citizen of the United Kingdom, residing at 78 Hardwick Road,

Ashland, Massachusetts 01721 hereby declare as follows:

Serial Number: 09/587,111

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Group Art Unit: 1646

(1) I am the inventor of the subject matter described and claimed in the above-identified application.

(2) Prior to January 22, 1999, the invention described and claimed in the above-referenced patent application was completed in this country, as evidenced by the following:

(a) Prior to January 22, 1999 I had completed the sequencing of the full length human VR-2 (SEQ ID NO:5) as evidenced by copies of the assembled contig map and the complete sequence of SEQ ID NO:5 derived from the contig map. The contig map and sequence print-out are submitted herewith as Exhibits A and B, respectively.

(b) Prior to January 22, 1999 I had determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor based on the results of a blast search using the amino acid sequence of SEQ ID NO:5. The top hit in this blast search analysis is rat vanilloid receptor 1 (VR-1; accession number AF029310). Based on the percent identity and percent similarity between the polypeptide of SEQ ID NO:5 and rat VR-1, and the fact that rat VR-1 was the top hit in the blast search analysis I determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor. The results of the blast search analysis are submitted herewith as Exhibit C.

(c) Prior to January 22, 1999, I had determined that the polypeptide of SEQ ID NO:5 represents a unique target for pain and that it may be responsible for hypersensitivity in chronic neuropathic pain, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule. The Qualified Target Summary Sheet is submitted herewith as Exhibit D.

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(d) According to my routine practice, immediately after identifying the polypeptide of SEQ ID NO:5 as a vanilloid receptor (hVR-2) associated with pain and classifying it as a Qualified Target, I contemplated routine uses of this molecule such as: (i) use of the molecule in screening assays to identify modulators of the vanilloid receptor or (ii) use of this molecule in the diagnosis of conditions/diseases associated with, for example, aberrant vanilloid receptor (hVR-2) nucleic acid expression or activity, e.g., pain disorders, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule.

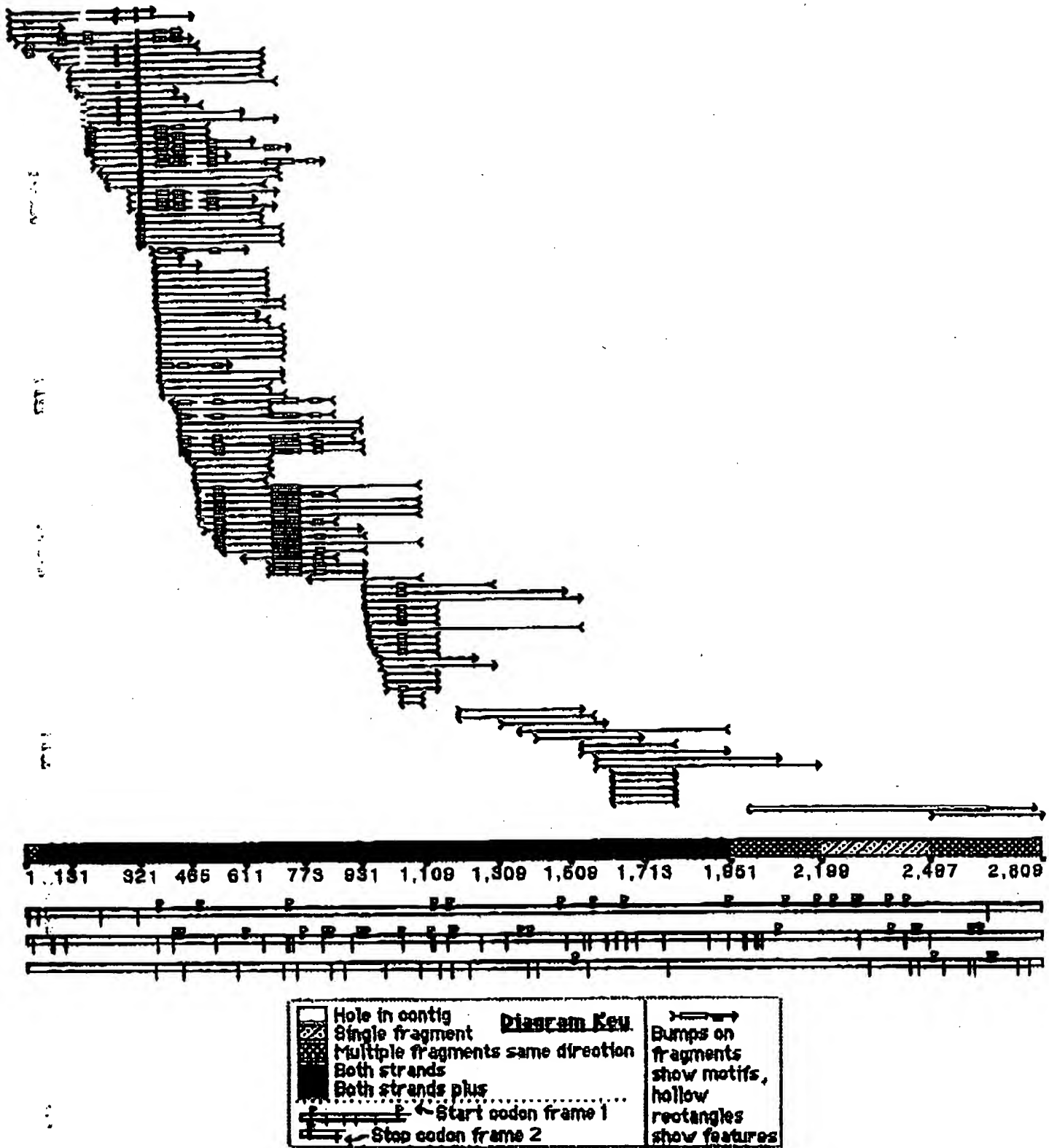
(e) The dates deleted from the contig map (Exhibit A), the sequence print-out (Exhibit B), the blast search results (Exhibit C), and the Qualified Target Summary (Exhibit D) are prior to January 22, 1999.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Rory Curtis  
Rory A.J. Curtis, Ph.D.

4/10/2003  
Date

## Exhibit A

21ella  
Sequencher™ "21ellracefinal"

## Exhibit B

21ella  
Sequencher™ "21ellracefinal"

flh21ell12 #1 GGCTAGCCTG TCCTGACAGG GGAGAGTTAA GCTCCCGTTC TCCACCGTGC CCGCTGQCCA GGTGGGCTGA GGGTGACCGA GAGACCAAGAA  
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T . . . . . T . . . . . T . . . . . T . . . . .

[illegible]

21ella  
Sequencer™ "21ellracefinal"

2 jchsa103p2v2 >#1>

TO

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[illegible]

21ella  
Sequencher™ "21ell1racefinal"

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21ella  
Sequencher™ "21ellafinal"

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+ + . . . . . T + + . . . . . + + . . . . . + + . . . . . + + . . . . .

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21e11a

Sequencer™ "21a11racefinal"

[illegible]

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21ella  
Sequencher™ "21ellracefinal"

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22 Flh21e11r14 0125 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ

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0811 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ  
L V N A Q C T P D Y Y R Q H S A L H I A I E K R S L Q C V K

(901) CTCTGTGTGG AGAATGGGGC CAATGTGCAT GCCCCGGGCTT GCGGCGCGCTT CTTCAGAGAG GGGCAAGGGA CTTCGTTTTA TTTGGGTGAG  
L L V E N G A M V N A R A C G R F Y Q K G Q G T C F Y F G E

#1081 ACTGACTCCC AGGGCAACAC AGTCCTGCAT GCCCTAGTGA TGATCTCGGA CAACTCAGCT GAGAACATTG CACTGGTGAC CAGCATGTAT  
T D S Q G N T V L H A L V M I S D N S A E N I A L V T S N Y  
T T T T

21ella  
Sequences "21ellracefinal"

1231 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
1231 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
1231 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
1231 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
Gembank AA3... 1289 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
Gembank AA3... 1289 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
jchla029c10c... >127  
Gembank W38... >127

11171 GATGGGCTCC TCCAAAGCTGG GGGCCGCTTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG  
D G L L Q A G A R L C P T V Q L E D I R N L Q D L T F L X L

1231 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCA  
1231 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
1231 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
1231 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
Gembank AA3... 1279 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
jchla029c10c... 127 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
Gembank W38... 1265 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
Gembank AA3... >127

11261 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG  
A A K E G E I E I P R H I L Q R E Y S G L S H L S R K P T E

1231 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
1231 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
1231 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
1231 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
Gembank W38... 1255 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
Gembank AA35... 1238 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
1231 GGGCTGTGCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
Gembank W38... 1242

11351 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAAGCTCAG TGCTGAGAT CATTCGCTTT  
W C Y G P V R V S L Y D L A S V D S C S E H S V L E I I A F

1501 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG C  
1501 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
1493 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
jchla029c10c... 1247 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
Gembank W38... 1245 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
Gembank AA3... 1228 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
1231 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
Gembank W38... 1242 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG

11441 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG  
H C K S P H R H R H V V L E P L H K L L Q A K W D L L I P E

21ella  
Sequencher™ "21ellracefinal"

Adm21ell - #425 GGCCTAAGC CAGATGGCAG CCCGGATGAG CGCTGGTGCT TCAGGGTGA GAGGTGAAC TGGGCTTCAT GGGAGCAGAC GCTGCTACG  
frmb12c4d1 - #415 TCAT GGGAGCAGAC GCTGCTACG

#2431 GGCCTAAGC CAGATGGCAG CCCGGATGAG CGCTGGTGCT TCAGGGTGA GAGGTGAAC TGGGCTTCAT GGGAGCAGAC GCTGCTACG  
G T K P D G S P D S R W C P X V E E V N W A S W S Q T L P T

Adm21ell - #515 CTCTGTGAGG ACCCGTCAGG GGCAGGTCTC CCTCGAATC TCAGAGACCC TGTCTGCT TCCCTCCCA AGGAGGATGA GATGGTGGC  
frmb12c4d1 - #25 CTCTGTGAGG ACCCGTCAGG GGCAGGTCTC CCTCGAATC TCAGAGACCC TGTCTGCT TCCCTCCCA AGGAGGATGA GATGGTGGC

#2531 CTCTGTGAGG ACCCGTCAGG GGCAGGTCTC CCTCGAATC TCAGAGACCC TGTCTGCT TCCCTCCCA AGGAGGATGA GATGGTGGC  
L C E D P S G A G V P R T L E N P V L A S P P E E D E D G A

Adm21ell - #605 TCTGAGGAAA ACTATGTGCC CGTCCAGCTC CTCCAGTCCA ACTGATGGCC CAGATGCAGC AGGAGGCCAG AGGACAGAGC AGAGGATCTT  
frmb12c4d1 - #115 TCTGAGGAAA ACTATGTGCC CGTCCAGCTC CTCCAGTCCA ACTGATGGCC CAGATGCAGC AGGAGGCCAG AGGACAGAGC AGAGGATCTT

#2611 TCTGAGGAAA ACTATGTGCC CGTCCAGCTC CTCCAGTCCA ACTGATGGCC CAGATGCAGC AGGAGGCCAG AGGACAGAGC AGAGGATCTT  
S E E N Y V P V Q L L Q S N W P H C S R R P E D R A E D L

Adm21ell - #695 TCCAACCACA TCTGCTGGCT CTGGGTTCCC AGTGAATTCT GGTGGCAAAT ATATATTTTC ACTAACTCAA AAAAAAAAAA AAAAA  
frmb12c4d1 - #205 TCCAACCACA TCTGCTGGCT CTGGGTTCCC AGTGAATTCT GGTGGCAAAT ATATATTTTC ACTAACTCAA AAAAAAAAAA AAAAA

#2701 TCCAACCACA TCTGCTGGCT CTGGGTTCCC AGTGAATTCT GGTGGCAAAT ATATATTTTC ACTAACTCAA AAAAAAAAAA AAAAA  
B N H I C W L W G F S E P W W Q I Y I P T M S K K K K K K K

frmb12c4d1 - #295 AAAAAAAAAA AAAAAAAAAA

#2791 AAAAAAAAAA AAAAAAAAAA  
K K K K K K

## Exhibit C

BLASTP vs. PNU (AA) flh2lellorfaa - 5:26:57 pm on Dec 21 98

BLASTP 1 4.10MP-WashU [30-Aug-96] [Build 20:24:58 Oct 21 1996]

Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Query= flh2lellorfaa  
(764 letters)

Database: /disk0/asap/databases/db/WRP/protxnu  
345,099 sequences; 106,000,184 total letters.  
Searching.....done

| Sequences producing High-scoring Segment Pairs:               | High<br>Score | Smallest<br>Sum<br>Probability<br>P(N) | N |
|---|---------------|--|---|
| GP:gi 2570933 (AF029310) vanilloid receptor subtype 1 [Ra...  | 336           | 1.9e-221                               | 7 |
| GPU:gi 3986159 gnl PID d1035925 (AB015231) VR1sk [Mus mus...  | 299           | 9.8e-136                               | 6 |
| GP:gi 2911863 (AF047660) contains similarity to ankyrin r...  | 103           | 6.5e-20                                | 8 |
| GP:gi 3675319 gnl PID e1344970 (Z74030) similar to ankyri...  | 97            | 1.1e-19                                | 7 |
| GP:gi 2642590 (AF031408) olfactory channel [Caenorhabditi...  | 93            | 3.6e-16                                | 6 |
| GP:gi 2854148 (AF045639) contains similarity to ankyrin r...  | 93            | 4.1e-16                                | 6 |
| GP:gi 3879753 gnl PID e1349345 (Z72514) Similarity to Hum...  | 73            | 3.6e-11                                | 6 |
| GP:gi 3267188 gnl PID e315126 (Y10601) ankyrin-like prote...  | 71            | 2.7e-08                                | 6 |
| SP:SP:sp P48994 TRPL_DROME TRANSIENT-RECEPTOR-FCNTENTIAL L... | 69            | 2.2e-05                                | 4 |
| GP:gi 1841966 (U65916) ankyrin [Rattus norvegicus]            | 72            | 5.6e-05                                | 3 |

WARNING: Descriptions of 4 database sequences were not reported due to the limiting value of parameter V = 11.

>GP:gi|2570933 (AF029310) vanilloid receptor subtype 1 [Rattus norvegicus]  
Length = 838

Score = 336 (156.0 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
Identities = 67/112 (59%), Positives = 84/112 (75%)

Query: 206 FYFGELPLSLAACTKQWDVVSYLENEHQPASLQATDSQGNVTLHALVMISDNSEAENIAL 265  
FYFGELPLSLAACT C +V +LL+N QPA + A DS GNTVLHALV ++DN+ +N  
Sbjct: 245 FYFGELPLSLAACTNQLAIVKBLQNSWQPADISARUSVENTVLHALVEVADNTVDNTKF 304

Query: 266 VTSMYDGLLQAGARLCPTVQLEDIRNLQDLTFLKLAKEGKIBIFRHILORE 317  
VTSMY+ +L GA+L PT++LE+I N + LTPL LAA GKI + +ILORE  
Sbjct: 305 VTSMYNEILILGAKLHPTLKLREITNRKGLTPLALAASSGKIGVLAYILORE 356

Score = 316 (146.7 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
Identities = 65/138 (47%), Positives = 93/138 (67%)

Query: 66 ASQPDPNRFRDRFLFNAVSRGVPEDLAGLFEYLSKTSKYLTDSEYTEGSTGKTCILMKAVL 125  
A + P +DR +F+AV++ ++L L +L ++ K LTDSE+ + TGKTCIL+KA+L  
Sbjct: 104 AGEKPFRLYDRRSIFDAVAQSNQCELESLL+FLQSKKRLTDSEFKDPETGKTCILKAML 163

Query: 126 NLKDGVNACILPLLIQIDRDSGNFQPLVNAQCTDDYYRGHSALHIAIEKRSIQCVKLLVEN 185  
NL +G N I LL + R + + + VNA TD YY+G +ALHIAIE+R++ V LLVEN  
Sbjct: 164 NLHNCQNDTIALLLDVARKTDSLKQFVNAS+TDSYYKGQTALHIAIEFRNMTELVTLLEN 223

Query: 186 GANVHARACGRFPQKQGQ 203

GA+V A A G FF+K +G

Sbjct: 224 GADVQAAANGDFFKKTG 241

Score = 299 (138.8 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
 Identities = 69/175 (39%), Positives = 94/175 (53%)

Query: 391 FFLNELCNLIYMFISTAVAYHOPTLKKAAAPHLKAEVGNMMLLTGHILILLGGIYLLVGQL 450  
 F+ NF +YM IFTA AY++P LK VG+ +TG IL + +

Sbjct: 434 FYFNFFVYCLYMIIFTAAAYYRFVEGLEFPYKLNKTVGDYFRVTGEILSVXXXXXXXKGI 493

Query: 451 WYFWRHVFIIWISFIDSVEILFLFQALLKPVSVLCLFLATEWYLPILLVSALVLGWLNL 510  
 YF +R + F+DSY EILF Q+L VS VL F + Y+ +V +L +GW N+L

Sbjct: 494 QYFLQRRPSLKSLEFVDSYSEILFFVQSLF+LVSVLYFSQRKEYVASMVFLAMGWITNL 553

Query: 511 YYTRGFQHTGIYSVMIOKVILRDLRPLLIYLVFLPGFAVALVSLSQEAWRPEAP 565  
 YYTRGFQ GIY+VMI+K+ILRDL R A+V+L ++ P

Sbjct: 554 YYTRGFQMGIVAVMIKMIILRDLRXXXXXXXKXTAVVTLIEDGKNNSLP 602

Score = 281 (130.5 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
 Identities = 54/95 (56%), Positives = 70/95 (73%)

Query: 586 GAQYRGILEASLELFKFTIGMGELAFQQLHFRGMVLLILLAYVLLTYILLNMLIALME 645  
 G Y + LELFKFTIGMG+L F E F+ + +LLAYV+LTYILLNMLIALM

Sbjct: 624 GNSYNSLYSTCLELFKFTIGMGDLFTENYDFKAVFIILLAYVILTYILLNMLIALMG 683

Query: 646 ETVNSVATDSWSIWKLOKAIISVLEMENGYWWCRKK 680  
 ETVN +A +S +IWKLO+AI++L+ E + C +K

Sbjct: 684 ETVNKIAQESKNIWKLOKRAITILDTEKSFLKCMRK 718

Score = 162 (75.2 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
 Identities = 28/38 (73%), Positives = 34/38 (89%)

Query: 323 HLSRKFTWCYGFVRVSLYDLASVDSCEZNSVLEIIAP 360  
 HLSRKFTFW YGPV SLYDL+ +D+CE+NSVLE+IA+

Sbjct: 364 HLSRKFTWAYGPFVHSSLYDLSCIDTCEKNSVLEVIAY 401

Score = 144 (66.9 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
 Identities = 25/47 (53%), Positives = 31/47 (65%)

Query: 678 RKKQBRAGVMTVGTKEPDGSPDERWCPRVEEVNWSWEOTLPTLCEDF 724  
 RK R+G +L VG EDG D RWCPRV+EVNW +W + + EDP

Sbjct: 717 RKAFRSGKLLQVGSTPDGKDDYRWCFRVEVNWTWNTNVGIINEDF 763

Score = 94 (43.6 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221  
 Identities = 15/30 (50%), Positives = 24/30 (80%)

Query: 363 KSPHRHRMVLEPLNKLQAKWDLIPKFF 392  
 ++P+RH M+++EPLN+LLQ KWD + + F

Sbjct: 405 ETPNRHDMILLVEPLNRLLODKWDRFVKRIF 434

Score = 46 (21.4 bits), Expect = 1.3e-162, Sum P(6) = 1.3e-162  
 Identities = 11/48 (22%), Positives = 24/48 (50%)

Query: 435 HILILLGGIYLLVGQLWYFWRHVFIIWISFIDSVEILFLFQALLKPV 482  
 H ++L+ + L+ W + + +F + F+ + I+F A +FV

Sbjct: 410 HDMILLVEPLNRLLODKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 457

Score = 37 (17.2 bits), Expect = 2.4e-169, Sum P(7) = 2.4e-169  
 Identities = 8/22 (36%), Positives = 13/22 (59%)

Query: 297 PLKLAKEGKIZIPRHILQREZ 318  
 PL LAA ++ I + +IQ +

Sbjct: 251 PLSLAACNTQLAIVKFLQNSW 272

Score = 37 (17.2 bits), Expect = 1.9e-111, Sum P(7) = 1.9e-111  
Identities = 8/26 (30%), Positives = 15/26 (57%)

Query: 206 FYFGELPLSLAACTKQWDVVSYLEN 231  
+Y G+ L +A + +V+ L+EN  
Sbjct: 198 YXGQTALHIAIERRNMTLVTLIVEN 223

>GPU:gi|3986159|gnl|PID|d1035925 (AB015231) VR1sk [Mus musculus]  
Length = 563

Score = 299 (138.8 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136  
Identities = 69/175 (39%), Positives = 94/175 (53%)

Query: 391 FFLNFLCNLIYMPIFTAVAYHQPTLKKAAPHKAEVGNMILLTCHILILLGGIYLLVGQL 450  
F+ NF +YM IPTA AY++P LK VG+ +TG IL + +  
Sbjct: 127 FYFNFVYCLYMIIFTAAAYRFEVGLPPYKLNVTGVDYPRVTGEILSVXXXXXXXXXRG 186

Query: 451 WYPWRRHVPIWISFIDSYPFELFLQALLKPVSOVLCLALIEWVLPLVLSALVLGWLNL 510  
YF +R + P+DSV RILF Q+L VS VL F + Y+ +V +L +GW N+L  
Sbjct: 187 QYFLQRRPSLKSFLVDSYSEILFFVQSLFMLVSVVLYFSQRKEVVASNVFSLANGWINML 246

Query: 511 YYTRGFQHTGIYSVMIOKVILRDLLRELLIYLVFLFGFAVALVSLSQAWRPEAP 565  
YYTRGFQ GIY+VMI+K+ILRD L A+V+L ++ P  
Sbjct: 247 YYTRGFQOMGIYAVMIKMIILRDLCRXXXXXXXXXXXXTAVVTLIEDGKNNSLP 301

Score = 253 (117.5 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136  
Identities = 50/89 (56%), Positives = 64/89 (71%)

Query: 586 GAQYRGILEASLELFKFTIGMGELAFQEQHFRGMVLLLLLAYVLLTYILLINMLIALMS 645  
G Y + LELEKFTIGMG+L P E F+ + +LLAYV+LTYILLINMLIALM  
Sbjct: 317 GNSYNSLYSTCLELFKFTIGMGDLFTENYDFKAVFIILLAYVILTYILLINMLIALMG 376

Query: 646 ETVNSVATDSWSIWKLQKALSULEMENGY 674  
ETV V+ +S IWKLQ A ++L++E +  
Sbjct: 377 ETVGQVSKESKHIWKLQWATTILDIERSF 405

Score = 163 (75.7 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136  
Identities = 28/47 (59%), Positives = 34/47 (72%)

Query: 678 RKKQRAGVMLTVGTPDGSPDERWCPRVEEVNWSWEQTLPTLCEDP 724  
RK R+G M+TVG DG+PD RWCPRV+EVNW+ W Q L + EDP  
Sbjct: 410 RKAFRSGEMVTVGKSSDGTDPDRRWCPRVDEVNWSHWNQNLGIINEDP 456

Score = 162 (75.2 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136  
Identities = 28/38 (73%), Positives = 34/33 (89%)

Query: 323 HLSRKFTWCYGPVRVSLYDLASVDSCEENSLEIIAP 360  
HLSRKFTW YGFP SLYDL+ +D+CE+NSVLE+IA+  
Sbjct: 57 HLSRKFTWYGPVHSSLYDLSCIDTCEKNSVLEVIAY 94

Score = 129 (59.9 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136  
Identities = 27/49 (55%), Positives = 36/49 (73%)

Query: 269 MYDGLLQAGARLCPTVQLEDIRNLQDLTPLKLAKEGKIEIFRHILORE 317  
MY+ +L GA+L PT++LE+I N + LTPL LAA GKI + +ILORE  
Sbjct: 1 MYNEIILGAKLHPTLKLREETNRKGLTPLALAASSGKIGVLAYILORE 49

Score = 94 (43.6 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136  
Identities = 15/30 (50%), Positives = 24/30 (80%)

Query: 363 KSPHRHRMVVLEPLNKLLOAKWDLLIPKFP 392

Query: 98 ETPNRHDMLLVEPLNRLLOQKWDKRVKRI 127  
 Score = 46 (21.4 bits), Expect = 2.3e-77, Sum P(5) = 2.3e-77  
 Identities = 11/46 (22%), Positives = 24/46 (50%)

Query: 435 HILILGGIYLLVQQLWYFWRHVFIIWISFIDSYPFELFLQALLKPV 482  
 H ++L+ + L+ W + + +P + E+ + I+E A +PV  
 Sbjct: 103 HDMLLVEPLNRLLOQKWDKRVKRIYFNFFVYCLYMIIFTAAAYRPV 150

Score = 42 (19.5 bits), Expect = 1.2e-122, Sum P(6) = 1.2e-122  
 Identities = 9/22 (40%), Positives = 16/22 (72%)

Query: 209 GELPLSLAACTKQWDVVSYLLE 230  
 G PL+LAA + + V++Y+L+  
 Sbjct: 26 GLTPLALAASSGKIGVLAYILQ 47

>GF:gi|2911863 (AF047660) contains similarity to ankyrin repeats  
 [Caenorhabditis elegans]  
 Length = 900

Score = 103 (47.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20  
 Identities = 23/29 (25%), Positives = 44/29 (49%)

Query: 497 LLVSALVLGWLNLIIYYTRGFQHTGIYSVMIOKVILRDLLRFLIIYLVFLGFAVALVSL 556  
 L+ ++ ++ LYY R + G + +M+ +I D+ RF+LTY +PL GF+ + +  
 Sbjct: 592 LITVTMIFTTVHYLYYCRVIRFVGPFVLMVYTIATDIFRFLIYGIPLMGFSQSFSLIF 651

Query: 557 QEAWRPEAPTGPNTESVQPMEGQEEDGN 585  
 R + + EG +++ N  
 Sbjct: 652 LSCEREANVIKKLITDOSEASEGSDNKEN 680

Score = 63 (29.3 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20  
 Identities = 15/27 (55%), Positives = 18/27 (66%)

Query: 291 NLQDLTFLKLAKEGRIEIRHILQRE 317  
 N Q L+PL LAAK K E+F IL+ E  
 Sbjct: 328 NKQSLSPILTIAAKLAKKEMFDEILELE 354

Score = 56 (26.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20  
 Identities = 16/48 (33%), Positives = 25/48 (52%)

Query: 151 LVNAOCTODVYRHSALHIAIEKRSLOQVALLVENGANVHARACGRFP 158  
 L+N + + G S LH AI + V ++ GA+V++R G FF  
 Sbjct: 185 LLNDIHTISZDFYGLSPLHQAIINTDCKLVYKFLKLGADVNSRCYGAF 232

Score = 54 (25.1 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20  
 Identities = 12/23 (52%), Positives = 13/23 (56%)

Query: 207 YFGELPLSLAACTKQWDVVSYLL 229  
 Y GE PLS AAC Q + LL  
 Sbjct: 263 YLGEYPLSFAACLNQPEPRLL 285

Score = 49 (22.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20  
 Identities = 8/23 (34%), Positives = 12/23 (52%)

Query: 331 WCYGPVRVSLYDLASVDSCEPNS 353  
 W YG + Y LA +D+ E +  
 Sbjct: 359 WAYGDASSTAYPLAKIDTINETT 381

Score = 47 (21.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20  
 Identities = 11/30 (36%), Positives = 18/30 (60%)

Query: 236 ASLOATDSQGNVTLHALVMISDENSENIAL 265  
 A+ A D+ GN+VLH V+ + + +AL  
 Sbjct: 289 ANFNAQDTNGNSVLHMCVIHENMAMFKLAL 318

Score = 46 (21.4 bits), Expect =  $5.7e-15$ , Sum P(6) =  $5.7e-13$   
 Identities = 9/27 (33%), Positives = 17/27 (62%)

Query: 163 GHSALHIAIEKRSLOQCVKLLVENGANV 189  
 G+S LH+ + ++ KL +E GA++  
 Sbjct: 298 GNSVLHMCVIHENMAMFKLALCCGASL 324

Score = 43 (20.0 bits), Expect =  $6.5e-20$ , Sum P(8) =  $6.5e-20$   
 Identities = 8/18 (44%), Positives = 13/18 (72%)

Query: 634 ILLNMLIALMSETVNSV 651  
 I+ NMLIA+M+ T ++  
 Sbjct: 753 IMQFNMLIAMCTTETI 770

Score = 41 (19.0 bits), Expect =  $6.5e-20$ , Sum P(8) =  $6.5e-20$   
 Identities = 10/27 (37%), Positives = 16/27 (59%)

Query: 113 GSTGKTCLMKAVLNKDGVNACILPLL 139  
 GS G+T + +L+ D NA +L +L  
 Sbjct: 153 GSMGETIIGCCILHASDIENALVLKIL 179

Score = 35 (16.3 bits), Expect = 0.00016, Sum P(3) = 0.00016  
 Identities = 9/37 (24%), Positives = 16/37 (43%)

Query: 67 SQPDPNRFRDRRLFNAVSRGVPEDLAGLPEVLSKTSK 103  
 S+P P R+ ++ V + GL E+ S+  
 Sbjct: 464 SEFFFRGRYGKNSTLQOVKPVINATSRGLVEWSEPLSQ 500

Score = 34 (15.8 bits), Expect =  $6.8e-11$ , Sum P(8) =  $6.8e-11$   
 Identities = 8/31 (25%), Positives = 17/31 (54%)

Query: 422 LKAEVGNMMLTGHILILGGIYLLVGQLWY 452  
 L ++ +L+ ++LI + I+ V L+Y  
 Sbjct: 577 LACDLSPVLLVVDNVLITVTMIPTTVHYLY 607

>GP:gi|3675319|gnl|PID|e1344970 (274030) similar to ankyrin repeats  
 [Caenorhabditis elegans] >GP:gi|3876480|gnl|PID|e1346172 (272508)  
 similar to ankyrin repeats [Caenorhabditis elegans]  
 Length = 790

Score = 97 (45.0 bits), Expect =  $1.1e-19$ , Sum P(7) =  $1.1e-19$   
 Identities = 18/53 (33%), Positives = 32/53 (60%)

Query: 497 LLVSALVLGWLNLIIYYTRGFQRTGIYSVMIQKVILRDLLRPLLIYLVFLFGFA 549  
 + + +++L + LYY R G + +M+ +I DL+RF +IY +FL GF+  
 Sbjct: 526 MAIISILLVTQHFLYYMRAIPFVGPFVLMVYTIATDLVRFAMIVSIFLVGFS 578

Score = 89 (41.3 bits), Expect =  $1.1e-19$ , Sum P(7) =  $1.1e-19$   
 Identities = 19/48 (39%), Positives = 27/48 (56%)

Query: 151 LVNAQCTDDYYRGHSALHIAIEKRSLOQCVKLLVENGANVHARACGRFF 198  
 L+N C + Y G S LH+AI + Q LL+ GA+++ R G FF  
 Sbjct: 189 LINDICVSEYVGLSPLHLAIVNQDAQFTSILLRLGADLNQRCYGAFF 236

Score = 62 (28.8 bits), Expect =  $1.1e-19$ , Sum P(7) =  $1.1e-19$   
 Identities = 13/23 (56%), Positives = 14/23 (60%)

Query: 207 YFGELPLSLAACTKQWDVVSyll 229  
YFGE PLS A C Q D+ LL  
Sbjct: 267 YFGEYPLSPAICMGQHDLFRL 289

Score = 51 (23.7 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19  
Identities = 10/19 (52%), Positives = 13/19 (68%)

Query: 236 ASLQATDSQGNLTVLHALVM 254  
A+L A D+ GNT LH V+  
Sbjct: 293 ANLSAQDTMGNTALHLCVI 311

Score = 49 (22.6 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19  
Identities = 11/51 (21%), Positives = 27/51 (52%)

Query: 601 KPTIGNGELAFQEQHFRGMVLLLLAYVLLTYILLNMLIALMSETVNSV 651  
+E++ E++ + + + L+ + + IL N+LIA+M+ T ++  
Sbjct: 626 EFSVLRYREMSACDNFWMKWLKIFVIFET+SILOFNLLIAMMTRTYETI 676

Score = 43 (20.0 bits), Expect = 1.2e-06, Sum P(5) = 1.2e-06  
Identities = 7/27 (25%), Positives = 16/27 (59%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANV 189  
G++ALH+ + + +E G N+  
Sbjct: 302 GNTALHLCVIHDKMDMLDAVLEAGNT 328

Score = 39 (18.1 bits), Expect = 5.5e-12, Sum P(7) = 5.5e-12  
Identities = 12/56 (21%), Positives = 25/56 (44%)

Query: 461 WISFIDSYPEILFLFOALLKPVSVQLCFIAIEWYLLVLSALVLGWLNLLYYTRGF 516  
W +E+ ++ L A L + + C LA ++ L + +++L T+ S  
Sbjct: 483 WFNFLKAPPAKLMFKGASLFIIISIPCLACSFHEFFLTIDNTMAIISILLVTOHF 538

Score = 38 (17.6 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19  
Identities = 9/18 (50%), Positives = 12/18 (66%)

Query: 289 IRLQDITPLKLAARKPK 306  
+ N Q+LT L LAA+ K  
Sbjct: 330 LANKQNLTAITLAARLAK 347

Score = 37 (17.2 bits), Expect = 4.7e-18, Sum P(7) = 4.7e-18  
Identities = 7/15 (46%), Positives = 9/15 (60%)

Query: 723 DPGAGVPRITLENPV 737  
DP G+ +ENPV  
Sbjct: 599 DPMGSEFNNTMENPV 613

Score = 36 (16.7 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19  
Identities = 10/47 (21%), Positives = 16/47 (34%)

Query: 376 LNKLLQAKWDLIPKFFLNFLCNLIYMFISTAVAYHQPTLKKAAPHL 422  
+ ++L KW +L L I+ + AY HL  
Sbjct: 362 IEQILDEKWKAYGRALWLSLLGFIFPYCCFVCAYMLRPSSATTEHL 408

Score = 35 (16.3 bits), Expect = 3.0e-08, Sum P(6) = 3.0e-08  
Identities = 9/23 (39%), Positives = 11/23 (47%)

Query: 207 YFGELPLSLAACTKQWDVVSyll 229  
Y+G PL LA + S LL  
Sbjct: 199 YYGLSPLHLAIVNQDAQFTSLLL 221

Score = 34 (15.8 bits), Expect = 3.9e-12, Sum P(5) = 3.9e-12  
Identities = 7/21 (33%), Positives = 13/21 (61%)

Query: 297 PLKLAKEGKIEIPRHILQRE 317  
 PL A G+ ++FR +L ++  
 Sbjct: 272 PLSFAICMGQHDLFRMLLAKK 292

Score = 34 (15.8 bits), Expect =  $8.9e-10$ , Sum P(7) =  $8.9e-10$   
 Identities = 6/18 (33%), Positives = 12/18 (66%)

Query: 610 AFQEQLHFRGMVLLLLLA 627  
 AF +L F+G L +---  
 Sbjct: 489 APPAKLMFKGAPLFIIIS 506

Score = 34 (15.8 bits), Expect =  $4.0e-08$ , Sum P(6) =  $4.0e-08$   
 Identities = 11/40 (27%), Positives = 16/40 (40%)

Query: 153 NAOCTDDYYRGHSALHIAIEKRSLOQCVKLLVENGANVHAR 192  
 N T Y G L AI ++L+ AN+ A+  
 Sbjct: 259 NTNYTGSMYFGEYPLSFAICMGQHDLFRMLLAKKANLSRQ 298

>GP:gi|2642590 (AF031408) olfactory channel (Caenorhabditis elegans)  
 Length = 937

Score = 93 (43.2 bits), Expect =  $6.8e-16$ , Sum P(5) =  $6.8e-16$   
 Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 GHSALHIAIEKRSLOQCVKLLVENGANVHARACGRFF 198  
 G SALH+AI + V LL+ + A+V+ARACG FF  
 Sbjct: 172 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 207

Score = 92 (42.7 bits), Expect =  $6.8e-16$ , Sum P(5) =  $6.8e-16$   
 Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMICKVILRDLLRFLLIYLVFLPGFA 549  
 L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+  
 Sbjct: 500 LFVVALPGSWIFLLFFARSAKLTGFVQMTYSMIAGDMIRFAIISAIFLVSFS 552

Score = 57 (26.5 bits), Expect =  $6.8e-16$ , Sum P(5) =  $6.8e-16$   
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230  
 Y+GE FL+ AAC D+ L++  
 Sbjct: 226 YYGEYPLAFAACFGNKKDIYDLLIQ 249

Score = 50 (23.2 bits), Expect =  $6.8e-16$ , Sum P(5) =  $6.8e-16$   
 Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTPLKLAKEGKIEIPRHILQ 315  
 N TPL LA K G+ +IF +L+  
 Sbjct: 294 NHAGFTPLTLATKLGKQIFREMLE 318

Score = 44 (20.4 bits), Expect =  $6.8e-16$ , Sum P(5) =  $6.8e-16$   
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 DSQGNVTIHALVMISDNDAENIAL 265  
 DS GNT+LH V+ +S +A+  
 Sbjct: 258 DSPGNTILHMCVINYSMSYSYAV 281

Score = 37 (17.2 bits), Expect =  $2.2e-05$ , Sum P(4) =  $2.2e-05$   
 Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231  
 FG+ L LA ++ VS LL +  
 Sbjct: 171 FGQSALHLAIVHDDYETVSLLLNS 194

Score = 34 (15.8 bits), Expect =  $3.6e-16$ , Sum P(6) =  $3.6e-16$   
 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384  
 +P M+ E + +LL KW  
 Sbjct: 363 TPEHLDMIGSEVIQRLADKW 383

>GP:gi|2854148 (AF045639) contains similarity to ankyrin repeats  
 [Caenorhabditis elegans]  
 Length = 957

Score = 93 (43.2 bits), Expect =  $7.6e-16$ , Sum P(5) =  $7.6e-16$   
 Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 GHSALHTAIEKRSIQCVKLLVENGANVHARACGRFF 196  
 G SALH+AI + V LL+ + A-V+ARACG FF  
 Sbjct: 175 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 210

Score = 92 (42.7 bits), Expect =  $7.6e-16$ , Sum P(5) =  $7.6e-16$   
 Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLIIYYTRGFQHTGIYSVMIOKVILRLIRFLLIYLVFLFGFA 549  
 L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+  
 Sbjct: 503 LFPALPGSWIFLLFFARSAKLTGPFVQMIYSMIAGDMIRFAIISAIPLVSFS 555

Score = 57 (26.5 bits), Expect =  $7.6e-16$ , Sum P(5) =  $7.6e-16$   
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230  
 Y+GE PL+ AAC D+ L++  
 Sbjct: 229 YYGEYPLAFACFGNKKDIYDLLIQ 252

Score = 50 (23.2 bits), Expect =  $7.6e-16$ , Sum P(5) =  $7.6e-16$   
 Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTFLKLAKEGKIEIPRHILQ 315  
 N TPL LA K G+ +IF +L+  
 Sbjct: 297 NHAGFTPLTLATKLGRKQIFPEEMLE 321

Score = 44 (20.4 bits), Expect =  $7.6e-16$ , Sum P(5) =  $7.6e-16$   
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 DSQGNITVLHALVMISDNSAENIAL 265  
 DS GNT+LH V+ +S + A+  
 Sbjct: 261 DSFGNTILHMCVINYSSEMYSYAV 284

Score = 37 (17.2 bits), Expect =  $2.4e-05$ , Sum P(4) =  $2.4e-05$   
 Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231  
 FG+ L LA ++ VS LL +  
 Sbjct: 174 FGQSALHLAIVHDDYETVSLLLNS 197

Score = 34 (15.8 bits), Expect =  $4.1e-16$ , Sum P(6) =  $4.1e-16$   
 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384  
 +P M+ E + +LL KW  
 Sbjct: 366 TPEHLDMIGSEVIQRLADKW 386

>GP:gi|3879753|gnl|PID|e1349345 (272514) Similarity to Human ankyrin  
(SW:ANK1\_HUMAN) (Caenorhabditis elegans)  
Length = 519

Score = 73 (33.9 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11  
Identities = 17/36 (47%), Positives = 19/36 (52%)

Query: 163 GHSALHIAIEKRSLSQCVKLLVENGANVHARACGRFF 198  
G S LK AI L+ V L GA+VH R G FF  
Sbjct: 186 GLSPLHQAIVNEDLENVYFLCRKGADVHQRCVGSFF 221

Score = 63 (29.3 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11  
Identities = 12/17 (70%), Positives = 13/17 (76%)

Query: 207 YFGELPLSLAACTKQWD 223  
Y+GE PLS AACT Q D  
Sbjct: 252 YWGEYPLSFAACTNQVD 268

Score = 52 (24.1 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11  
Identities = 13/27 (48%), Positives = 17/27 (62%)

Query: 289 IRNLQDLTFLKLAKEGKIEIFRHLQ 315  
+RN LTPL LAA+ K I+ IL+  
Sbjct: 315 VRNNLKLTPALAAARLAKKHIDLILE 341

Score = 51 (23.7 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11  
Identities = 10/22 (45%), Positives = 12/22 (54%)

Query: 331 WCYGPFVRVSLYDLASVDSCEEN 352  
W YGPV Y L VD+ E+  
Sbjct: 348 WRYGPFVCKAYFLNDVDITNES 369

Score = 43 (20.0 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11  
Identities = 8/13 (61%), Positives = 10/13 (76%)

Query: 242 DSQGNITVLHALVM 254  
D+ GNTVLH V+  
Sbjct: 284 DTNGNTVLHLTVI 296

Score = 37 (17.2 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11  
Identities = 8/35 (22%), Positives = 16/35 (45%)

Query: 376 LNKILQAKWDLIPKFFINFLCNLIYMFIF+VAY 410  
+ ++L++KW+ K L IY +A+  
Sbjct: 398 IEEVLESKWETFOKKQLFMSLAGYIYFLAVFYLA 432

>GP:gi|3287188|gnl|PID|e315126 (Y10601) ankyrin-like protein [Homo sapiens]  
Length = 1119

Score = 71 (33.0 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08  
Identities = 13/30 (43%), Positives = 20/30 (66%)

Query: 163 GHSALHIAIEKRSLSQCVKLLVENGANVHAR 192  
G++ LH A+EK ++ VK L+ GAN + R  
Sbjct: 98 GNTPLHCAVEKNQIESVKFLLSRGANPNLR 127

Score = 63 (29.3 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08  
Identities = 10/30 (33%), Positives = 20/30 (66%)

Query: 501 ALVLGWLNLVYTRGFQHTGIYSVMIOKVI 530  
A+ W+N L Y + F++ GI+ VM++ ++  
Sbjct: 638 AVYFYWMNLYLQRPENCGIFIVMLEVIL 667

Score = 59 (27.4 bits), Expect =  $9.0e-07$ , Sum P(6) =  $9.0e-07$   
Identities = 10/30 (33%), Positives = 19/30 (63%)

Query: 167 LHIAIEKRSIQCVKLLVENGANVHARACGR 196  
LH+A++ L+ +K+ ++NGA + GR  
Sbjct: 243 LHLAVQNGDLEMIMCLDNGAQIDPVEKGR 272

Score = 50 (23.2 bits), Expect =  $2.7e-08$ , Sum P(6) =  $2.7e-08$   
Identities = 10/26 (38%), Positives = 18/26 (69%)

Query: 291 NLQDLTFLKLAKEGKIEIFRHILQR 316  
+L +TFL LAAG G ++ +L++  
Sbjct: 479 DLHGMTPLHLAAKNGHDKVQVQLLLKK 504

Score = 49 (22.8 bits), Expect =  $2.7e-08$ , Sum P(6) =  $2.7e-08$   
Identities = 10/26 (38%), Positives = 14/26 (53%)

Query: 209 GELPLSLAACTKQWDVVSYLLZNPHQ 234  
G PL LA + W++V+ LL Q  
Sbjct: 342 GRSPLILATASASWNIUNLLLSKGAQ 367

Score = 48 (22.3 bits), Expect =  $3.2e-05$ , Sum P(5) =  $3.2e-05$   
Identities = 9/32 (28%), Positives = 20/32 (62%)

Query: 524 VMIOKVILRDLLRFLLIYLVFLFGFAVALVS 555  
+++ +VIL+ LLR +++++ L F ++ +  
Sbjct: 860 IVMLEVILKTLRSTVVFIPLLLAFGLSPYIL 891

Score = 41 (19.0 bits), Expect =  $2.7e-08$ , Sum P(6) =  $2.7e-08$   
Identities = 9/28 (32%), Positives = 15/28 (53%)

Query: 525 MIOKVILRDLLRFLLIYLVFLFGFAVAL 552  
+I K +LR + P+ + L F F + L  
Sbjct: 865 VILKTLRSTVVFIPLLLAFGLSPYIL 892

Score = 40 (18.6 bits), Expect =  $2.9e-07$ , Sum P(5) =  $2.9e-07$   
Identities = 13/50 (26%), Positives = 24/50 (48%)

Query: 620 MVLLLLLAYVLLTYILLNMLIALMSETVNSVATDSWSIWKLQKAISVLE 669  
+V + LL L++ +LLN+ S ++ + T S + + S LE  
Sbjct: 875 VVFIFPLLLAFGLSPYILNLDQPFSSPLLSIIQTFSSMLGDINYRESFLE 924

Score = 40 (18.6 bits), Expect =  $7.6e-05$ , Sum P(5) =  $7.6e-05$   
Identities = 8/19 (42%), Positives = 12/19 (63%)

Query: 296 TPLKLAKEGKIEIFRHIL 314  
TPL LA + G +B+ + L  
Sbjct: 241 TPLHLAVQNGDLEMIMCL 259

Score = 39 (18.1 bits), Expect =  $2.7e-08$ , Sum P(6) =  $2.7e-08$   
Identities = 7/19 (36%), Positives = 14/19 (73%)

Query: 623 LLAYVLLTYILLNMLIAL 643  
L+++ + I+L+N+LI L  
Sbjct: 941 LVSFTIFVPIVLMNLLIGL 959

Score = 39 (18.1 bits), Expect =  $6.8e-07$ , Sum P(6) =  $6.8e-07$   
Identities = 9/36 (25%), Positives = 18/36 (50%)

Query: 293 QDLTFLKLAKEGKIEIFRHILQRFFSGLSHLSRKF 328  
+ LT L + +IE+ H + +E+ + L+ F  
Sbjct: 681 EPLTALNAMVQNNRIELNHPVCKEYLLMKWLAYGF 716

Exhibit D



## Qualified Target Summary Sheet

|  |  |
|--|--|
|  | <b>Vanilloid Receptor Homologue (VR-2)</b>   |
| <b>CFA Disease Area (s):</b>           | Pain   |
| <b>Druggable Target Class:</b>         | Calcium channel  |
| <b>MPI Gene Sequence Identifier:</b>   | Fh21e11 (Mine 18560)   |
| <b>Top Blast Hit:</b>                  | Rat vanilloid receptor 1 (VR1)   |
| <b>Amino Acid Coding Region:</b>       | ORF: 361-2652  |
| <b>CDNA Length:</b>                    | 2806 bp  |
| <b>Source (Tissue / Cell Line):</b>    | First clone identified in an internal heart library  |
| <b>Novel / Unrecognized:</b>           | ? Unrecognized / Novel   |
| <b>% Novelty:</b>                      | 66% novel across the complete cDNA.<br>Hits unannotated sequence in Non-Public Patent Data Base  |
| <b>Patent Status:</b>                  | Filed Nov. 1, 1998   |
| <b>Full Length Clone:</b>              | Yes  |
| <b>Expression Profiling Results:</b>   | Present in a sub-population of sensory neurons different from VR1.<br>Also present in sympathetic neurons.   |
| <b>Background:</b>                     | The published vanilloid receptor (Caterina et. Al. Nature 389:816-24, 1997) responds to heat and capsaicin by activating $Ca^{++}$ influx in sensory neurons (Tominaga et.al., Neuron 21: 531-43, 1998). Capsaicin also binds to this channel. |
| <b>Hypothesis:</b>                     | This channel may be responsible for hypersensitivity in chronic neuropathic pain and represents a unique target for pain.  |
| <b>Assay Type:</b>                     | Cell-based assay   |
| <b>Reagents Needed:</b>                | Open reading frame will be cloned by Millennium into pCDNA 3.1   |
| <b>Readout:</b>                        |  |
| <b>Critical Experiments Necessary:</b> |  |

**MPI Target Name:**

Vanilloid Receptor Homologue (VR-2)

**QT Nomination Date:**

12/22/98

**Action Taken:**

Accepted QT (unrecognized) Pending full length cDNA

**Date Accepted:**

**Bayer QT Leader:**

Rory Curtis or Peter DiStefano

**MPI QT Leader:**


**BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE  
UNITED STATE PATENT AND TRADEMARK OFFICE**

**LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)**

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**Expires: August 5, 2003**

  
\_\_\_\_\_  
Harry I. Moatz  
Director of Enrollment and Discipline